2. Claims 51-55 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-22 of U.S. Patent 5,122,464.

While not agreeing with this rejection, Applicants respectfully submit that a terminal disclaimer may be provided upon indication that the pending claims are allowable.

3. Claims 56-58 stand rejected under 35 USC § 112, second paragraph, as being indefinite in the recitation of "reduced".

The Examiner asserts that the term "reduced" is subjective and could include a cell which produces 99.99% of normal GS activity.

Applicants respectfully traverse this rejection and submit that the definition of "reduced" is clear to anyone reading the specification because this term has a well recognized definition. For instance, Webster's New World Dictionary (3rd College Edition) defines "reduced" as "to lessen in any way, as in size, weight, amount, value, price, etc.; diminish" (a copy of this page is attached as exhibit A).

The Examiner states that this term could encompass cells which produce 99.99% of normal GS activity to cells producing 0.001% of normal GS activity. Applicants respectfully agree with the Examiner that the term "reduced" encompasses the stated levels of GS activity. Applicants respectfully direct the Examiner to the preamble of claim 56 which recites: "A method of endowing a cell line with the ability to survive in a medium

(08/302,241)

lacking glutamine...". According to this limitation of claim 56, it is the vector which endows the cell line with the ability to survive in glutamine-free medium. Therefore, the endogenous levels of glutamine are not an issue.

Applicants respectfully submit that the level of endogenous GS activity is not a limiting factor in the claimed method as vector encoded GS is a dominant selectable marker wherein cells expressing endogenous levels of GS can be selected against by the use of GS inhibitors such as Msx (see page 9, first paragraph of the specification). Applicants have shown that selection for gene amplification using Msx leads almost exclusively to the isolation of clones in which the vector-derived GS gene has been amplified over the endogenous gene (see page 9, second paragraph of the specification).

Applicants respectfully submit that the test for indefiteness is whether one skilled in the art would understand the bounds of the claim when read in light of the specification.

Miles Laboratories, Inc. v. Shandon Inc., 27 USPQ2d 1123, 1126, 997 F.2d 870 (Fed. Cir. 1993). If the claims read in light of the specification reasonably apprise those skilled in the art of the scope of the invention, § 112, second paragraph demands no more. Id. Given this test for indefiteness and the fact that GS is a dominant selectable marker, the recitation of "reduced" levels of GS in the claimed method of endowing a cell line with the ability to survive without glutamine cannot be held to be

(08/302,241)

indefinite. Accordingly, Applicants respectfully request withdrawal of the above identified rejection.

CONCLUSIONS

In view of the above discussion and Amendments, Applicants respectfully submit that the application is considered to be in condition for allowance. The Examiner is invited to call the undersigned attorney if any minor matter remains.

Respectfully submitted,

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ExhibitA

THIRD COLLEGE EDITION

Webster's New World Dictionary

OF AMERICAN ENGLISH

VICTORIA NEUFELDT

Editor in Chief

DAVID B. GURALNIK

Editor in Chief Emeritus



Webster's New World Cleveland & New York tell

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spuralist] a larval stage of many trematodes, usually perasitic in a spiralist produced by a sporocyst and producing daughter rediae or

ndiscount rate athe rate of interest charged by a district Federal Reserve Bank for rediscounting top-grade commercial paper offered

With member banks

Glistrib-ute (re'dis trib'yoot, -yoot) vt. -uted, -ut-ing to distribute

again or in a different way. -re'dis-tri-bu'tion a. -re'dis-trib'u-tive

rdistrict (re distrikt) vt. to divide anew into districts, esp. so as to reapportion electoral representatives

making paint, in glassmaking, etc. ind-letter (red'let'er) adj. designating a memorable or joyous day or

wants from the custom of marking holidays on the calendar in red

id ight 1 any danger or warning signal; specif., a red lamp, flare,

red-light district (red'lit') a district (in a town or city) containing many brothels: brothels in such districts formerly displayed red

bred lin ing (red'lin in) n. I from the practice of outlining such areas in red on a map I the systematic refusal by some lending institutions of insurance companies to issue mortgage loans or insurance on ripoperty in certain neighborhoods regarded by them as deteriorating man an North American Indian: sometimes an offensive term and meat meat that is red before cooking; esp., beef or mutton as detinguished from prok yeal poultry etc.

distinguished from pork, veal, poultry, etc.

fedneck or red-neck (red/nek) n. [from the characteristic sunbuild neck acquired in the fields by farm laborers] [Slang] a poor,

white, rural Southerner, often, specif, one regarded as ignorant, bigoted, violent, etc.

ddness (nis) n. the state or quality of being red (do (re do o') vt. -did', -done', -do'ing 1 to do again or do over 2 to freeorate (a room, etc.)

system (a room, etc.)

synd Oak 1 any of several oaks having leaves with sharp-tipped those dark bark, and acorns which require two years to mature 2 the reddish, hard wood of such a tree of ocher a red, earthy hematite, used as a pigment.

Adolence (red ons) n. the quality or state of being redolent Also charteness.

int olency — SYN. SCENT

int olency — SYN. SCENT

colent (-ent) add. [OFr < L redolens, prp. of redolere; to emit a

lent; < re(d)-, intens. + olere; to smell (akin to odor, odor)] 1

rest smelling fragrant 2 smelling (of) 'fredolent of the ocean' 3

regestive or evocative (of) — red'olently adv.

don (re don'), Odd-lon (8 de lon') 1840-1916; Fr. painter & lithog
miner: **The county of the county of the

dondo Beach (re dän'do bech') [< Sp redondo, circular, round +

nd Osier 1 a shrubby dogwood (Cornus stolonifera) with dark-red cinches and white or bluish fruit 2 any of several willows with

dinches and white or blush Iruit 2 any of the state of th wint value or penalty of a bid which an opponent has doubled upon "redouble" when it is one's turn to bid —n. Bridge a

count (ri dout') n. [Fr redoute < It ridotta < ML reductus, refuge, is pp. of L reducere: see REDUCE] 1 a) a breastwork outside a long transfer of the country of the coun mation 2 any stronghold

Diable (-a bal) adj. [ME redowtable < MFr redoutable <

1125

red-hot / reduce

redouter, to fear, dread < L re-, intens. + dubitare, to DOUBT 1 formidable; fearsome [a redoubtable foe] 2 commanding respect [a redoubtable logician] —re-doubt'a|bly sdv.
re-dound (ri dound') vl. [ME redounden < MFr redonder < L redundare, to overflow < re(d)-, intens + undare, to surge, swell < unda, a wave: see WATER 1 to have a result or effect (to the credit or discredit, etc. of someone or something) 2 to come back; react; recoil (upon): said of honor or disgrace 3 [Obs.] to surge up or overflow

red out (red'out') n. [RED + (BLACK)OUT] a blurring of vision, as if by a red mist, caused by the forcing of blood into the head during feet-first acceleration, as in flying

re-dox (re'daks') n. [< red(uction-)ox(idation)] Chem. OXIDATION-

REDUCTION

REDUCTION

red pepper 1 any of various capsicums having a many-seeded green

fruit that turns red when it is ripe: see CAPSICUM 2 the fruit

red pine a wide spreading pine (Pinus resinosa) of the NE U.S., with

glossy, green needles in groups of two

red-poll (red'poll) n. [RED + POLL] any of a number of finches (genus

Acanthis) with a red patch on the head and a black chin

Red Poll (pol) any of a breed of medium-sized, reddish beef and dairy

cettle with no horse originating in Navious and Suffolk counties

cattle with no horns, originating in Norfolk and Suffolk counties, England

England
re-draft (re'draft', -draft', for v. re draft', -draft') n. 1 a second or
later draft or framing, as of a legislative bill 2 a new draft on the
original drawer or endorser of a protested bill of exchange, for the
amount of the bill plus charges and costs — vt. to draft again or anew
re-dress (ri dres'; for n., usually re'dres') vt. [ME redressen < OFr
redrecier: see RE- & DRESS] 1 to set right; rectify or remedy, often
by making compensation for (a wrong, grievance, etc.) 2 [Now
Rare] to make amends to —n. 1 a compensation or, satisfaction, as
for a wrong done 2 the act of redressing — SYN. REPARTION —
redress the balance (or scales) to make a fair adjustment; see that
justice is done — re-dress'able adj. — re-dress'er n.
re-dress (re'dres') vt. to dress again
*red-root (red'root', -root') n. any of various plants with red roots, as

*red-root (red'root', -root') n. any of various plants with red roots, as
a) a small shrub (genus Ceanothus) of the buckthorn family b) a marsh plant (Lachnanthes tinctoria) of the bloodwort family, with sword-shaped leaves and flat clusters of small, woolly, yellow flowers, found along the Atlantic coast of the U.S. c) PIGWEED (sense 1) d) BLOODROOT

red salmon sockeye salmon

Red Sea sea between NE Africa & W Arabia, connected with the Mediterranean Sea by the Suez Canal & with the Indian Ocean by the Gulf of Aden: c. 1,400 mi. (2,253 km) long: c. 178,000 sq. mi.

(461,000 sq. km)
red shank (red shank') n. either of two European sandpipers with

reddish legs, esp. the more common species (Tringa totanus)
red shift the relationship between the positions of spectral lines from
the light of near and distant luminous bodies in which the greater
the distance, the greater the shift toward the longer wavelengths and lower frequencies at the red end of the spectrum; Hubble effect: thought to be a Doppler effect which would indicate motion away

from the earth, as in an expanding universe *red shirt (red'shert) vt. [from the traditional red shirts worn by the scrimmage team, with whom such players may continue to practice] [Slang] to withdraw (a player) from a varsity team for a year so that the player will be eligible for athletics an extra year later -n. such a player red siskin a South American finch (Carduelis cucullata) with a black

head and red body, sometimes kept as a cage bird

*red snapper 1 a reddish, edible, deep-water snapper fish (Lutjanus campechanus) of the Gulf of Mexico and W Atlantic 2 any of several other reddish fishes, as a rockfish (Sebastes ruberrimus) of the E Pacific

red spider any of a number of small spider mites that can defoliate

red squill 1 a variety of sea onion having red bulbs which yield a powder used chiefly in rat poison 2 this powder street squirrel a common North American tree squirrel (genus

Tamiasciurus) with reddish fur red start (start') n. [RED + obs. start < ME stert, tail < OE stert: see STARK-NAKED] *1 any of various wood warblers; esp. the American red start (Setophaga ruticilla), the male of which is black and orange above and white below 2 any of a genus (Phoenicurus) of small European thrushes with a reddish tail; esp. a common species (P. phoenicurus)

(P. phoenicurus)

red tape [after the tape commonly used to the official papers] 1

official forms and routines 2 rigid application of regulations and routine; resulting in delay in getting business done

★red tide a reddish discoloration of sea waters, caused by large numbers of red dinoflagellates (esp. genera Gymnodinium and Gönyaulax) that kill fish and other organisms by releasing poisonous prod-

red top (-tap') n. [from the reddish panicle of some forms] *a grass (Agrostis gigantea) grown in the cooler parts of North America for hay, pasturage, and lawns

re-duce (ri doos', -dyoos') vt. -duced', -duc'ing [ME reducen < L at, ate, car; ten, eve; is, lee; go, hôrn, look, tool; oil, out; up, fur; e for unstressed vowels, as a in ago, u in focus; 'as in Latin (lat'n); chin; she; zh as in azure (azh'er); thin, the; n as in ring (rin) In etymologies: " = unattested; < = derived from; > = from which & = Americanism See Inside front and back covers





reducere, to lead back < re-, back + ducere, to lead: see DUCT | 1 a) to lessen in any way, as in size, weight, amount, value, price, etc.; diminish b) to put into a simpler or more concentrated form 2 to bring into a certain order; systematize 3 to break up into constituent elements by analysis 4 a) to put into a different form /to reduce a talk to writing b) to change to a different physical form, as by melting, crushing, grinding, etc. 5 to lower, as in rank or position; demote; downgrade 6 a) to bring to order, attention, obedience, etc. as by persuasion or force b) to subdue or conquer (a city or fort) by siege or attack 7 a) to bring into difficult or wretched circumstances siege or attack I a) to bring into difficult or wretched circumstances fa people reduced to poverty) b) to compel by need to do something freduced to stealing 8 a) to weaken in bodily strength; make thin freduced to skin and bones b) to thin (paint, lacquer, etc.), as with turpentine 9 Arith. to change in denomination or form without changing in value fto reduce fractions to their lowest terms 10 Chem. a) to decrease the positive valence of (an element or ion) b) to increase the number of electrons of (an atom, element, or ion) c) to remove the oxygen from; deoxidize d) to combine with hydrogen at the first into the matellie state by removing nonmetallie elements. e) to bring into the metallic state by removing nonmetallic elements 11 Phonet. to articulate (a vowel) in a central position, giving it a neutral quality, as in an unstressed syllable 12 Photog. to weaken or lower the density of (a negative or print) by removing metallic silver 13 Surgery to restore (a broken bone, displaced organ, etc.) to normal position or condition -vi. 1 to become reduced 2 to lose

mal position or condition —v. 1 to become reduced 2 to lose weight, as by dieting —SYN. DECREASE—re-duc'ibil'ity n.—re-duc'ible adj.—re-duc'ibly adv.
re-duc|er(-ar) n. 1 a person or thing that reduces 2 Mech. a fitting for connecting two pipes of different size 3 Photog. a solution that dissolves silver, used to decrease the density of a negative or positive

reducing agent any substance that reduces another substance, or brings about reduction, and is itself oxidized in the process reducing glass a biconcave lens used for reducing the visual size of

something viewed through it

something rewest through it
re-duc-tase (ri duk'tās', -tāz') n. [REDUCT(ION) + -ASE] any of a class
of enzymes that catalyze biochemical reductions

re-duc-tijo ad ab-sur-dum (ri duk'të ô' ad ab sur'dəm, -shē ô') | L, reduction to absurdity \(\) Logic the proof of a proposition by showing its opposite to be an obvious falsity or self-contradiction, or the disproof of a proposition by showing its consequences to be impose or absurd

re-duction (ri duk'shan) n. [LME reduction < MFr reduction < L reductio < reductus, pp. of reducere 1 1 a reducing or being reduced 2 anything made or brought about by reducing, as a smaller copy, lowered price, etc. 3 the amount by which anything is reduced —re-

duc'tional adj.
reduction division MEIOSIS (sense 1)

re-duc-tion-ism (-iz'em) n. any method or theory of reducing data, processes, or statements to seeming equivalents that are les plex or developed: usually a disparaging term —re-duc'tion ist n., adj. —re-duc'tion is' fic adj. re-duc'tive (ri duk'tiv) adj. [ML reductivus] 1 of or characterized

by reduction or reductionism 2 reducing or tending to reduce -

re-duc-tor (-ter) n. Chem. any apparatus for carrying out the reduction of metallic ions in solution for purposes of analysis; specif., a long tube filled with granular zinc for reducing a ferric solution to its

re-dun-dan'cy (ri dun'den se) n., pl. -cies [L redundantia] 1 the state or quality of being redundant; superfluity 2 a redundant quantity; overabundance 3 the use of redundant words 4 the part of a redundant statement that is superfluous 5 [Brit., etc. (exc. Cdn.)] discharge from a job or employment because of not being needed; dismissal Also re dun'dance

dismissal Also re-dun'dance
re-dun-dant (-dant) adj. [L redundans, prp. of redundare: see
REDOUND] 1 more than enough; overabundant; excess; superfluous
2 using more words than are needed; wordy 3 unnecessary to the
meaning: said of words and affixes 4 [Brit., etc. (exc. Cdn)] laid off
from work as no longer needed; discharged; dismissed — SYN. wordy

from work as no longer needed; discharged; dismissed —374. words —re-dun/dantly adv.
re-du-pli-cate (ri dōo'pla kāt', -dyōo'-; for adj. & n., usually, -kit) vt.
-cat'ed, -cat'ing [< LL reduplicatus, pp. of reduplicare: see RE- & DUPLICATE] 1 to redouble, double, or repeat 2 a) to double (a root syllable or other element) so as to form an inflected or derived form of a word (as tom-tom), sometimes with certain changes, as of the vowel (as in chitchat) b) to form (words) by such doubling —vi. to be or become reduplicated —adj. 1 reduplicated; doubled 2 VAL-VATE (sepse 2n) —n. something reduplicated

be or become reduplicated —adj. 1 reduplicated; doubled 2 VALVATE (sense 2a) — n. something reduplicated
re-du-pli-ca-tion (ri dov)pla kā'shan, dyōv'.) n. [LL reduplicatio] 1
a reduplicating or being reduplicated 2 something produced by
reduplicating, as a word containing a reduplicated element 3 the
element added in a reduplicated word form —re-du'pli-ca'tive adj.
re-du-v||id (ri dov'vē id, -dyōv'.) n. [< ModL Reduvidae < L reduvia,
hangnail, remnant < OL redivia < *reduere, to strip away < red.

PRE - du-vere < [E hase *vur. to put on] assassin Buc

nangnail, remnant < OL redivia < *reduere, to strip away < red., RE- + -uere < IE base *eu-; to put on] ASSASSIN BUG redux (re'duks') adj. [L < reducere: see REDUCE] that has been brought back, revived, restored, etc. red-ware (red'wer') n. [RED + ware, seaweed < ME war < OE < IE *woiso-; twig, wand, rod < base *wei-; to twist, bend > wire] any of several large, brown, leathery, edible kelps (genus Laminaria) red water Texas rever

red wine any wine made from dark, purplish grapes when the grape

skins are left with the juice after pressing to allow the absorption reddish coloring agents during fermentation

red wing (-win) n. 1 a small European thrush (Turdus iliacu) an orange-red patch on the underside of the wings 22 RED-WING

BLACKBIRD Ared-winged blackbird a North American blackbird (Action of patch on each wing near the action) phoeniceus) with a bright-red patch on each wing near the should in the male Also redwing blackbird

in the male Also redwing blackbird red-wood (-wood') n. *1 a giant evergreen (Sequoia semperatural) of the baldcypress family, having fire-resistant bark, enduring and wood, and needlelike leaves: found in coastal regions of Californiand S Oregon *2 BIG TREE 3 any of a number of trees with redwood or yielding a red dye 4 the wood of any of these trees Redwood City city in W Calif., on San Francisco Bay: suburb of San Francisco: non. 55.000

Francisco: pop. 55,000

Redwood National Park national park in NW Calif., containing groves of redwood trees: 170 sq. mi. (440 sq. km) red worm BLOODWORM

re-echio or re-echio (re ek'ō) vt., vi. -ech'oed, -ech'oing to back or again; resound -n., pl. -ech loes the echo of an echo

re-ëch'o
reechly (rê'chē) adj. reech'i-er, reech'i-est [LME rechy < ME.
rechly (rê'chē) adj. reech'i-er, reech'i-est [LME rechy < ME.
red (rēd) n. [ME rede < OE hreod, akin to OHG hriot < IE be
'kreut-, to shake. tremble] 1 a) any of
various tall, slender grasses (esp. genus
Phragmités), with plumelike inflorescences, growing in wet or marshy land
b) the stem of eny of these grasses (e) h) the stem of any of these grasses c) such plants or stems collectively, specif. as material for thatching, basketwork, etc. 2 a rustic musical instrument made from a hollow stem or stalk and played by blowing through it 3 an ancient Hebrew unit of linear measure equal to 6 cubits: Ezek. 47:3 4 a device on a loom, by means of which threads are drawn between the separated threads of the warp 5 [Old Poet.] an arrow 6 Archit.

REEDS small, rounded molding; reeding 7 Music a) a thin strip of a a small, rounded moturing, recently a small, rounded moturing, recently a small, rounded moturing, recently a small placed against the opening of the module place of certain wind instruments, as the clarinet, so as to keep the control of the module and the recently as the clarinet, so as to keep the control of the module and the control of the control of the module and the control of the contr

decorate with reeds
Reed (red) 1 John 1887-1920; U.S. journalist & radical 2 Warned hird (-burd) n. dial. name for BOBOLINK

Reed (red) 1 John 1887-1920; U.S. journaust or radical a mod or rept 1851-1902; U.S. army surgeon & bacteriologist reed-bird (-burd') n. dial. name for Bobolink
reed-bird (-burd') n. pl. -buck' or -bucks' [transl. of Du ridde argain any of a genus (Redunca) of small African antelopes with spread hooves and, in the males, backward-sloping, ringed to the result of t

spread nouves and, in the mains, backward-stoping, iniged with turned inward and forward near the tips
reed ing (-in) n. 1 a small, rounded, decorative molding 2 and such moldings, as on a column 3 knurling along the edge of the construment any instrument whose sound is produced vibrating reed or reeds, including, specif., the oboe, clarinet, and the column of the reed instrument any instrument whose sound with a set of free metal reeds instead of professional reed or and bassoon reed mace Brit. name for CATTAIL reed organ an organ with a set of free metal reeds instead of professional reed organ and read organ with a set of free metal reeds instead of professional reed organ and organ with a set of free metal reeds instead of professional reed organ and organ with a set of free metal reeds instead of professional reed organ and organ with a set of free metal reeds instead of professional reed organ and organ with a set of free metal reeds instead of professional reed organ and organ with a set of free metal reeds instead of professional reed organ and organ with a set of free metal reeds instead of professional reed organ and organ with a set of free metal reeds instead of professional reed organ and organ with a set of free metal reeds instead of professional reed organ and organ with a set of free metal reeds instead of professional reed organ and organ with a set of free metal reeds instead of professional reed organ and organ with a set of free metal reeds instead of professional reed organ and organ with a set of free metal reeds instead of professional reed organ and organ with a set of free metal reeds instead of professional reed organ and organ with a set of free metal reeds instead of professional reed organ and organ with a set of free metal reeds instead of professional reed organ and organ with a set of free metal reeds instead of professional reed organ and organ with a set of free metal reeds instead of professional reed organ and organ with a set of free metal reeds instead of professional reed organ and organ with a set of free metal reeds instead of professional reed organ and organ with a set of free metal reeds instead of professional reed organ and organ with a set of free metal reeds instead of professional reed organ and reed organ and organ with a set of free metal reeds instead organ and organ and organ and organ and organ and organ and organ an

produce the tones: cf. REED PIPE reed pipe an organ pipe in which the tone is produced by a current air striking a vibrating reed in an opening in the pipe: cf. rust reed stop 1 a set of reed pipes (in an organ) operated by one the knob

re-ed|u|cate or re-ed|u|cate (rē ej's kāt') vt. -cat'ed, -cat'ed,

re-ed/uca/tive adj.
re-ed/

fumes, etc.) -reek'ly adj.

cound an VIRGINI

(rel) n.

VIRGINI

(rel) n.

trike, mal

rekls, shir etc. is pe, etc. us gral steel in to wi sh) by win sily and q to-reel so separat enforce INFORCE nter or ntrant o

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to turch

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OBOE REED (TOP VEW)

or, origin class, dat mination

mention, in names, s s (ref's re m 2 an or Law a po ce, and re my who e lo its fitn a dentials, see'inc ee'ing ice (ref'a

ity for